

**UNITED STATES DISTRICT COURT  
FOR THE DISTRICT OF MASSACHUSETTS**

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JOHN HANCOCK LIFE INSURANCE  
COMPANY, JOHN HANCOCK VARIABLE  
LIFE INSURANCE COMPANY, and  
MANULIFE INSURANCE COMPANY (f/k/a  
INVESTORS PARTNER INSURANCE  
COMPANY),

Plaintiffs,

vs.

ABBOTT LABORATORIES,

Defendant.

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Civil Action No. 05-11150-DPW  
Hon. Judge Douglas P. Woodlock

**ERRATA RE: DEFENDANT’S EXHIBIT 586 TO THE AFFIDAVIT OF  
JEFFREY MARC LEIDEN, MD., PH.D.**

Abbott Laboratories (“Abbott”) respectfully submits this Errata in connection with D’s Exhibit 586 to the Affidavit of Jeffrey Marc Leiden, MD., Ph.D., filed February 18, 2008 (“Leiden Affidavit”). Due to a copying error, Abbott inadvertently attached the wrong document as D’s Exhibit 586. A true and correct copy of the proper exhibit is attached hereto as D’s Exhibit 586. The courtesy copy of the Leiden Affidavit that Abbott is submitting to the Court will include the corrected D’s Exhibit 586.

ABBOTT LABORATORIES

By its attorneys

/s/ Eric J. Lorenzini

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Dated: February 20, 2008

**CERTIFICATE OF SERVICE**

I hereby certify that this document(s) filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of Electronic Filing (NEF) and paper copies will be sent to those indicated as non registered participants on February 20, 2008.

Date: February 20, 2008.

\_\_\_\_\_/s/ Eric J. Lorenzini

**D's Exhibit 586**

# ASCO 2001 MMPI Update

- Ten MMPI abstracts were presented
- Prinomastat, marimastat & Bay 12-9566 reported negative findings
- Possible reasons
  - Under dosing due to dose limiting toxicity (joint toxicity)
  - Inappropriate tumor selection
  - Inappropriate tumor stage (late vs. early)
  - Phase II development not done for prinomastat & Bay 12-9566
- BMS 275291 did not show joint toxicity in Phase I. Phase II studies are being initiated in NSCLC & Kaposi's sarcoma

# Prinomastat

- Non-small cell lung cancer
  - Combination with paclitaxel & carboplatin
  - No survival benefit
- Hormone refractory prostate cancer
  - Combination with mitoxantrone & prednisone
  - No effects on: PSA, progression free survival, overall survival
- Refractory metastatic breast cancer
  - Phase I/II single agent (n = 44)
- Grade 2 joint toxicity in above trials at all dose levels (5,10,25 mg bid)
- Studies in earlier stage tumors are still ongoing

# Marimastat

- Small cell lung cancer
  - Following response to 1<sup>st</sup> line therapy
  - 10mg vs. placebo
  - Total 155 patients
  - No benefit on progression free survival or overall survival
- Glioblastoma
  - Post surgery & radiotherapy
  - 10mg vs. placebo
  - Total 162 patients
- High dropout rate due to joint toxicity

# Bay 12-9566

- Ovarian cancer (stage III or IV)
  - 800mg bid vs. placebo
  - Study was discontinued prior to full enrollment due to lack of activity in pancreatic cancer and SCLC
  - No benefit on survival



# BMS 275291

- Phase I studies
  - Healthy volunteers (n = 40 males)
  - Cancer patients (n = 44)
- No joint toxicities (possibly due to lack of sheddase activity)
- No MTD through 2400mg / day
- Phase II plan
  - Non small cell lung cancer in combination with paclitaxel & carboplatin
  - Kaposi's sarcoma
  - Dose 1200 mg / day

# ABT-518 Phase I Multiple-Dose Study in Cancer Patients

## M00-235

- Patients enrolled to date
    - 25 mg / day
    - 50 mg / day
- |   |
|---|
| 4 |
| 3 |
| 7 |
- Dosing duration up to 57 days
  - Patients will continue dosing until disease progression or adverse events
  - No musculoskeletal effects reported to date
  - Next dose is 100 mg / day

# ABT-518 Development Recommendations

- Continue the ongoing Phase I study
  - Objectives
    - Determine target dose required to achieve target plasma concentration of 1-3  $\lambda$ M
    - Assess safety following chronic administration
- Stop development if Grade 3 or 4 toxicities are attributed to doses at or below target dose
- Stop for joint toxicity
- If target dose is well tolerated, initiate a pharmacodynamic/proof of principle study with external funds (e.g., NCI-CRADA) and/or outlicense
  - Biopsy multiple melanoma, head and neck cancer, assay for gelatinase A/B activity